



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/528,982

08/15/2005

James B. Doherty

21281 YSP

6373

210 7590 03/17/2008
MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER

NOLAN, JASON MICHAEL

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

03/17/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/528,982	Applicant(s) DOHERTY ET AL.	
	Examiner JASON M. NOLAN	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 March 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-4, 6-8 and 11 is/are rejected.
- 7) ☒ Claim(s) 5, 9, 10 and 12 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/23/05; 05/30/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This Office Action is responsive to Applicants Transmittal of New Application, filed 03/23/2005, (US filing date 08/15/2005). **Claims 1-12** are pending in the instant application.

Information Disclosure Statement

Applicants' information disclosure statements (IDS), filed on **03/23/2005** and **05/30/2006** have been considered. Please refer to Applicants' copies of the 1449 submitted herein.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-8 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In the case *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. § 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of **Claims 6-8** is a method for treating macular edema, macular degeneration, Alzheimer's disease, cognitive disorders, diabetes, etc. comprising the administration of a compound according to claim 1.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the

Art Unit: 1626

art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. *In the instant case*, the claimed invention is highly unpredictable since one skilled in the art would recognize that the compounds according to **Claim 1** may be useful for treating ocular diseases such as ocular hypertension, glaucoma, but it does not mean that the compounds according to **Claim 1** are useful for treating macular edema, macular degeneration, Alzheimer's disease, cognitive disorders, diabetes, etc.

The reference of Bhattacharyya *et al.* (*Current Eye Research* **2002**, 24(3), 173-181) establishes that, "Iberiotoxin, a specific maxi-K⁺ channel blocker antagonizes the action of the β -agonist (-)-isoproterenol. Since adrenergic agents decrease intraocular pressure possibly by reducing aqueous humor secretion from ciliary epithelial cells, our results indicate that membrane-derived G protein regulation of NPE maxi-K⁺ channels may play a role for modulation of intraocular pressure." Therefore, one of skill in the art would recognize that the compounds according to **Claim 1** may be useful for treating ocular pressure, but the use of maxi-K⁺ channel inhibitors for the treatment of diseases such as macular edema, macular degeneration, Alzheimer's disease, cognitive disorders, diabetes, etc. is not so advanced for this mechanism of action.

The breadth of the claims

The breadth of the **Claims 6-8** is a method for treating macular edema, macular degeneration, Alzheimer's disease, cognitive disorders, diabetes, etc. comprising the administration of a compound according to **Claim 1**. In short, the methods include a plethora of diseases.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine which compounds according to Formula I are potent Maxi-K⁺ channel inhibitors; determine which diseases (all of which have unique patient populations) are treatable via Maxi-K⁺ channel inhibitors; and conduct the trials necessary to establish the invention as enabling.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which compounds according to Formula I exhibit the desired pharmacological activity via the established mechanism of action.

Thus, the specification fails to provide sufficient support for the broad use of the compounds according to formula I for treating macular edema, macular degeneration, Alzheimer's disease, cognitive disorders, diabetes, etc.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001 states, “a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion” and “patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable”.

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to determine if the compounds according to formula I are useful for treating the plethora of diseases encompassed in the instant claims, with no assurance of success. This rejection can be overcome by deleting the claims.

Claim Rejections - 35 USC § 112

Claim 11 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Said claims recite the language: a prostaglandin “or derivative thereof” and the scope of this term is unclear, such that it fails to define the metes and bounds of its limitation. The term derivative is loosely bound and may refer, in essence, to any analog of the hundreds of synthetic prostaglandins made to date. For example, the examples listed in **Claim 12** define the metes and bounds of the claim. Examiner suggests cancelling **Claim 11** in light of **Claim 12** or using more descriptive terms such as those in **Claim 12**.

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 4 is rejected under 35 U.S.C. 101 as claiming the same invention as that of **Claim 7** of prior U.S. Patent No. **7,196,082**. This is a double patenting rejection.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over **Claims 1-3** of U.S. Patent No. **7,196,082**.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to overlapping subject matter. The compounds of the instant application are not patentably distinct from those of the '082 Patent because of substituents **X**, **Y**, **Q**, **R₂**, **R₃**, **R₄**, **R₅**, **R₆**, **p**, & **n**. In the '082 Patent: **Q** is **CR_y**; **X** can be **-(CHR₇)_pCO-**, **R₇** can be H, **p** is not 0; **Y** is **-CO(CH₂)_n**, **n** can be 0-3; and **R₆**. **Claim 3** of the '082 Patent directs the invention to **n = 0** as in the instant application.

Therefore, although the claims of the instant application are not identical to those of the '082 Patent, overlapping compounds directed towards the same methods of therapy are claimed.

Claim Objections

Claims 5, 9, 10, & 12 are objected to as being dependent upon a rejected base, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason M. Nolan, Ph.D.** whose telephone number is **(571) 272-4356** and electronic mail is Jason.Nolan@uspto.gov. The examiner can normally be reached on Mon - Fri (9:00 - 5:30PM). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph M^cKane** can be reached on **(571) 272-0699**. The fax phone number for the organization where this application or proceeding is assigned is **571-273-8300**. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Jason M. Nolan, Ph.D./

Examiner, Art Unit 1626

/Joseph K McKane/

Supervisory Patent Examiner, Art Unit 1626